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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,149	04/30/2001	Christian Schwabe	CONN-015CON	6580

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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,149	SCHWABE ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, claims 4-6, in the reply filed on 6-16-04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-3, 7-12 are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 4-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above

factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The nature of the invention is drawn to relaxin like factor peptide and methods of treating various diseases by the administration of relaxin like Polypeptides. The diseases include cardiovascular diseases, neurological or neurodegenerative disease, sinus bradycardia, depression, hair loss, or diseases related to uncontrolled or abnormal collagen or fibronectin formation. The invention is premised on the fact that the relaxin like factor "possesses relaxin-like biological activity and is therefore similarly implicated in" the treatment of diseases that can be achieved by relaxin (see page 13-14 of the specification).

(2) The state of the prior art

As a general proposition, it is not sufficient to conclude, based on the familial relationship, that a particular peptide will possess activity similar to other members of the group. That is because a difference in a few amino acids within the sequence can lead to divergent activities. Rudinger et al. States "[t]he significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study." Applicant's specification, on page 3, teaches that relaxin shares numerous structural features with the members of insulin related family of hormones. However, even with the similarities, the "proteins comprising the insulin-related family have been found to have distinct biological functions and activities. It has reported that this distinction is in large part a consequence of differences between a few type-specific amino acid residues. For example, the difference between

the glycine in position A14 of human type II relaxin and the isoleucine in the equivalent position of A(10) of insulin is considered a critical in distinguishing between the biological activity of the two proteins." (see page 3 of the specification).

Further, although there may be some similarity between activities of relaxin and relaxin like factor, a correlation between all activities attributed with relaxin to relaxin like factor cannot be made without undue experimentation. The art has recognized various drugs that, while in one instance have similar activity, in another instance they completely different activity. For example, Lidocaine and Mexiletine are known to be useful in the treatment of cardiovascular disorders such as arrhythmia. Although Mexiletine is an analog of Lidocaine, both drugs attribute different effects in the treatment of arrhythmias. Lidocaine is effective in treating Ventricular fibrillation, while Mexiletine is not. On the other hand, Mexiletine is effective in treating Ventricular arrhythmias in cardiomyopathy and Ventricular tachycardia while Lidocaine is not. It is known in the art that Lidocaine has substantial fist pass hepatic metabolism, while Mexiletine has similar electrophysioloic actions to Lidocaine, but has little or no first pass hepatic metabolism (see page 468 and 474 of the Merck Manual).

Even where the peptides recognize the same receptor, one cannot readily conclude that the compounds will exhibit similar activity. An example of this is the activity of IGF-1 and IGF-2. It is known that although both IGF-1 and IGF-2 recognize the Type I IGF receptor their activity can be quite different. For example, Klempt et al. teach that in a study involving the use of exogenous IGF-1 and IGF2 for the recovery of central nervous tissue after traumatic damage, such as asphyxia, it was found that IGF significantly reduced neural loss, but IGF-2 had no effect (see abstract).

Finally, the art recognizes that relaxin and relaxin like factor do not always recognize the same receptor. Luna et al. discloses that relaxin has a high affinity for LGR7 relaxin receptor.

However, as indicated by Silvertown et al., relaxin like factor, also known as INSL3, does not bind to this receptor (see page 514).

(3) The relative skill of those in the art

The relative skill of the those in the art is high.

(4) The predictability or unpredictability of the art

The true fact of the state of the art in peptide chemistry is expressed succinctly in the Rudinger article (see the conclusions in particular). "The significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study." Thus, the it is unpredictable to attribute activity of a peptide based on structure alone. Further, as indicated in the state of the prior art, it is also unpredictable to conclude activity of a peptide based on a familial relationship.

(5) The breadth of the claims

The claims are drawn to a method of treating a mammal for a condition susceptible to be treated with relaxin. The claims then specify numerous disorders that have been implicated as being treatable with relaxin. These disorders include, cardiovascular diseases, neurological or neurodegenerative disease, sinus bradycardia, depression, hair loss, or diseases related to uncontrolled or abnormal collagen or fibronectin formation.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples

The specification has not provided ample guidance as to the manner in which each disorder is to be treated or if truncated relaxin like factor would be effective in all of the disorders claimed. The extent of guidance provided in the specification is that the native peptide "Relaxin have been implicated consequently in the treatment and diagnosis of various diseases." Moreover, the specification only makes a suggestion in the treatment of all the disorders claimed without providing ample support as how and in what manner the disorders are treated. The specification is void of any working examples that would demonstrate beyond mere arguments that Relaxin Like peptides treat a specific disease in a specific manner.

As indicated in the state of the prior art, it is not sufficient to conclude that since relaxin like factor is structurally similar to relaxin, they possess similar activity. As Applicants specification indicates that proteins comprising the insulin-related family have been found to have distinct biological functions and activities, due in large part to the differences between a few type-specific amino acid residues.

It is noted that the specification basis its conclusions on the fact that relaxin and relaxin like peptide recognize similar receptors. Again, as indicated in state of the art, this proposition is not necessarily true. The art indicates while relaxin binds specifically to LGR7 receptor, relaxin like factor does not have the same binding affinity. In fact, relaxin like factor does not even bind to this receptor. Thus, one cannot readily conclude that based on the receptor binding activity both relaxin and relaxin like peptide will achieve the same activity. This is because relaxin and relaxin like factor have different receptor binding.

Moreover, assuming arguendo, that both relaxin and relaxin like factor bound to the same receptor, one cannot readily conclude that both will have similar activity. The art indicates that peptides that have similar binding receptors still have divergent activity. It is known that although

both IGF-1 and IGF-2 recognize the Type I IGF receptor their activity can be quite different. For example, Klempt et al. teach that in a study involving the use of exogenous IGF-1 and IGF2 for the recovery of central nervous tissue after traumatic damage, such as asphyxia, it was found that IGF significantly reduced neural loss, But IGF-2 had no effect (see abstract).

Finally, the claims also allow for the truncation of the peptides that are used to treat the disorders claimed. As stated by the Rudinger reference, "The significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study." The specification is void of any examples that would demonstrate that truncation of the peptide does not alter the activity of the peptides and thus are still useful in treating the claimed disorders.

(8) The quantity of experimentation necessary

Since applicants have not provided any guidance as to a specific condition to be treated for many of the disorders claimed, one of ordinary skill would burdened with undo experimentation to determine to what disorders the relaxin like polypeptide would be most effective in and conditions to treat. Even, for the specific disorders claimed one still would be burdened with undo experimentation to determine in what manner the conditions are to be treated. Taking all of the Wands factors as a whole, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the all of the peptide analogues would not affect the property of the peptide.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach

the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell, can normally be reached on (571) 272-0974. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

9/6/04

Anish Gupta
Patent Examiner